PATENT SPECIFICATION

NO DRAWINGS

Inventors: GEORGE MITCHELL GRASS Jr. and DONALD RICHARD MACDONNELL

1,097,955

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Date of Application and filing Complete Specification: Sept. 14, 1965.
No. 39279/65.
CompleteSpecification Published: Jan. 3, 1968.

Index at acceptance: —C3 T(6F2, 6H1, 6H4C, 6H4E, 6H4X); A5 B(2C, 2D, 2G, 2H, 2L, 2P)
Int. Cl.: —C 08 g 47/02

COMPLETE SPECIFICATION

PATENTS ACT, 1949

SPECIFICATION NO. 1,097,955

In accordance with the Decision of the Principal Examiner, acting for the Comptroller-General, dated 1st January, 1969 this Specification has been amended under Section 14 in the following manner:-

Page 1, line 45, *after* "antacid" *insert* "in the form of a compressed tablet"

Page 2, line 17, page 4, line 30, *delete* "acacia gum, guar gum,"

Page 2, line 19, *delete* "milk solids, polyvinyl alcohol, polyvinyl -" *insert* "and milk solids."

Page 2, *delete* lines "20 and 21"

Page 3, *delete* lines "3 to 50" inclusive

Page 3, line 51, *for* "Example G" *read* "Example D"

Page 3, *delete* lines "69 to 82" inclusive

Page 4, line 31, *after* "caseinate" in second occurrence *insert* "and"

Page 4, *delete* lines "32 and 33" *insert* "solids,"

Page 4, *delete* lines "50, 51 and 52"

Page 4, *for* claims "6 to 11" *read* "5 to 10" inclusive

Page 4, line 62, *for* "7" *read* "6"

Page 4, line 67, *for* "1 to 6" *read* "1 to 5"

Page 4, line 74, *for* "H" *read* "D"

THE PATENT OFFICE,
5th March 1969

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COMPLETE SPECIFICATION

An Organopolysiloxane-containing Tablet

We, SMITH KLINE & FRENCH LABORATORIES of 1500 Spring Garden Street, City of Philadelphia, Commonwealth of Pennsylvania, 19101, United States of America, a corporation organized under the laws of the Commonwealth of Pennsylvania, one of the United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement: —

This invention relates to a compressed tablet containing an antacid and a spray dried powdered organo-polysiloxane composition.

Recently, therapeutic uses have been revealed for organopolysiloxanes. In veterinary practice these compounds may be used for treating frothy bloat in ruminants and tympanic colic in horses. In humans the organopolysiloxanes are being used to treat gastrointestinal disturbances.

In the past, the organopolysiloxanes which are liquid or semi-solid were either supplied as an oil or an emulsion. Recently, solid forms of silicones have been prepared by adsorbing them on silica gels or other adsorbing agents. However, none of these forms of polyorganosiloxane is adapted for the proper dispersion which is necessary to obtain the full effect of the organopolysiloxane.

More recently, powdered organopolysiloxane compositions have been prepared and have been found to overcome the previous problems such as the difficulty of dispersion in aqueous sytems and in handling of the organopolysiloxane. These powder form compositions have made the compounds much more adaptable to specific situations.

It has now been discovered that the powdered organopolysiloxane composition as hereinafter described can be effectively used in the treatment of gastrointestinal disturbances if it is administered in conjunction with an antacid.

Accordingly the present invention provides a compressed tablet for the treatment of gastrointestinal disturbances, comprising pharmaceutically acceptable quantities of an antacid and a spray dried powdered organopolysiloxane composition as hereinafter described.

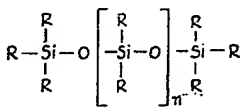
Among the antacids which can be used in the compressed tablet of the invention are magnesium aluminium oxyhydroxide, aluminium hydroxide dried gel, aluminium phosphate, calcium carbonate, magnesium carbonate, magnesium trisilicate, magnesium oxide, dihydroxy aluminium aminoacetate, magnesium hydroxide or a combination thereof.

In the compressed tablet the antacid and the organopolysiloxane composition may be separately contained in one or more layers or a coating, or they may be intimately mixed prior to compression.

In the preparation of a powdered silicone composition for use in the compressed tablet of the invention, an emulsion comprising the organopolysiloxane, a non-toxic coating material and water is prepared. The emulsion is then spray dried to form dry particles comprising the organopolysiloxane substantially completely coated with the coating material.

The organopolysiloxane used in making the spray dried composition will be in liquid form and will be present in an amount from 5% to 85% and preferably from 20% to 50% by weight of the powdered organopolysiloxane composition used in the tablet. Advantageously the oily or semi-solid organopolysiloxanes are represented by the general formula:

[*Pric*



where R represents a lower alkyl radical not exceeding 5 carbon atoms or a phenyl radical, and n can be from 0 to 2000. Most advantageously the siloxanes can be methylpolysiloxanes of at least 200 c.s. viscosity at 25°C., preferably with a viscosity of between 250 and 1000 c.s. at 25°C. Preferably the methylsiloxanes will contain from 1.9 to 2.1 methyl radicals per silicon atom.

The coating material for the organopolysiloxane used in the composition is present in an amount of from 15% to 95% and preferably from 50% to 80% by weight of the organopolysiloxane. The coating material for the organopolysiloxane will be selected from acacia gum, guar gum, calcium caseinate, sodium caseinate, ammonium caseinate, milk solids, polyvinyl alcohol, polyvinylpyrrolidone, methylcellulose and carboxymethylcellulose.

Preferably, the above noted coating materials for the organopolysiloxane will also act as emulsifying agents. However, if the specific coating material does not possess inherent emulsifying properties it can be mixed with other emulsifying coating material or with well known emulsifying agents such as sorbitan fatty acid esters and polyoxyethylene sorbitan fatty acid esters.

The spray drying is carried out in an apparatus which is conveniently used for spray drying and is well known to the art. The spray drying conditions may vary within wide ranges. It is, however, preferred to use a minimum inlet temperature of about 100°C. and a maximum outlet temperature of about 150°C. Preferably the inlet temperature will be higher than the outlet temperature and advantageously will be as high as the limitations will permit. Desirably during the course of operation the inlet and outlet temperatures remain substantially constant. The dried coated organopolysiloxane product is collected in a receiver at the bottom of the main chamber.

The spray dried powdered organopolysiloxane compositions which can be obtained in the manner hereinbefore described consist of substantially spherical dry particles, preferably of uniform particle size, comprising the organopolysiloxane substantially completely coated with one of the above-mentioned coating materials. The particle size is from 5 to 1000 microns and preferably from 20 to 100 microns.

The finished powdered organopolysiloxane composition formed from the above process can then be used in the preparation of the tablets of the invention.

As an indication of pharmaceutically acceptable quantities, the tablet of the invention will usually comprise from 0.1 to 1 g. of an antacid and from 10 mg. to 100 mg. of the spray dried powdered organopolysiloxane composition, as will be appreciated from the specific Example hereinafter described.

The following preparatory Examples illustrate the preparation of organopolysiloxane compositions which can be employed in the compressed tablet of the invention.

EXAMPLE A

Ingredients	Amounts
Methylcellulose, U.S.P. 15 cps	5 gms.
Milk Solids, Nonfat Dry	45 gms.
Dimethylpolysiloxane	50 gms.
Purified Water, U.S.P.	180 gms.

The methylcellulose is dispersed in the dimethylpolysiloxane. The milk solids are dissolved in water and the dispersion is added to the reconstituted milk and agitated to form an emulsion. The mixture is then homogenized to complete emulsification. This emulsion is then spray dried in a conventional spray dryer using an inlet temperature of 265°C. and an outlet temperature of at least 120°C. The product is then collected as a dry powder.

EXAMPLE B

Ingredients	Amounts
Methylcellulose, U.S.P. 15 cps	5 gms.
Milk Solids, Nonfat Dry	20 gms.
Dimethylpolysiloxane	75 gms.
Purified Water, U.S.P.	150 gms.

The methylcellulose is dispersed in the dimethylpolysiloxane. The milk solids are dissolved in water and the dispersion is added to the reconstituted milk and agitated to form an emulsion. The mixture is then homogenized to complete emulsification. This emulsion is then spray dried in a conventional spray dryer using an inlet temperature of 265°C. and an outlet temperature of at least 120°C. The product is then collected as a dry powder.

EXAMPLE C

Ingredients	Amounts
Carboxymethylcellulose	5 gms.
Dimethylpolysiloxane	50 gms.
Calcium Caseinate	45 gms.
Purified Water, U.S.P.	250 gms.

The carboxymethylcellulose is dispersed in the dimethylpolysiloxane and the calcium caseinate is dissolved in water and mixed with the dispersion. The mixture is then homogenized to complete emulsification. This emulsion is then spray dried in a conventional spray dryer using an inlet temperature of 265°C.

and an outlet temperature of at least 120°C. The product is then collected as a dry powder.

EXAMPLE D

Ingredients	Amounts
Polyvinyl Alcohol	15 gms.
Dimethylpolysiloxane	85 gms.
Purified Water, U.S.P.	250 gms.

The polyvinyl alcohol is dissolved in water with the aid of heat and the dimethylpolysiloxane is added. This mixture is then homogenized to complete emulsification. This emulsion is then spray dried in a conventional spray dryer using an inlet temperature of 265°C. and an outlet temperature of at least 120°C. The product is then collected as a dry powder.

EXAMPLE E

Ingredients	Amounts
Methylcellulose, U.S.P. 15 cps	5 gms.
Polyvinylpyrrolidone	45 gms.
Dimethylpolysiloxane	50 gms.
Purified Water, U.S.P.	150 gms.

The methylcellulose is dispersed in the dimethylpolysiloxane and the polyvinylpyrrolidone is dissolved in water and mixed with the dispersion. The mixture is then homogenized to complete emulsification. This emulsion is then spray dried in a conventional spray dryer using an inlet temperature of 265°C. and an outlet temperature of at least 120°C. The product is then collected as a dry powder.

EXAMPLE F

Ingredients	Amounts
Polyvinyl Alcohol	5 gms.
Dimethylpolysiloxane	40 gms.
Soy Bean Meal	55 gms.
Purified Water, U.S.P.	450 gms.

The polyvinyl alcohol is dissolved in water with the aid of heat and dimethylpolysiloxane is added to this and emulsified. The soy bean meal is added and cooked until the meal becomes hydrated and a smooth suspension results. This suspension is then homogenized to complete emulsification. This emulsion is then spray dried in a conventional spray dryer using an inlet temperature of 265°C. and an outlet temperature of at least 120°C. The product is then collected as a dry powder.

EXAMPLE G

Ingredients	Amounts
Methylcellulose, U.S.P. 15 cps	5 gms.
Milk Solids, Nonfat Dry	45 gms.
Phenylmethylpolysiloxane	50 gms.
Purified Water, U.S.P.	180 gms.

The methylcellulose is dispersed in the phenylmethylpolysiloxane. The milk solids are dissolved in water and the dispersion is added to the reconstituted milk and agitated to form emulsification. The mixture is then homogenized to complete emulsification. This emulsion is then spray dried in the conventional spray dryer using an inlet temperature of 265°C. and an outlet temperature of at least 120°C. The product is then collected as a dry powder.

EXAMPLE H

Ingredients	Amounts
Acacia	40 gms.
Sorbitan Monolaurate	2 gms.
Polyoxyethylene Sorbitan Monolaurate	8 gms.
Dimethylpolysiloxane	50 gms.
Purified Water, U.S.P.	400 gms.

The sorbitan monolaurate and polyoxyethylene sorbitan monolaurate are mixed with the dimethylpolysiloxane. The acacia is dissolved in the water and added to the oil phase. The mixture is then homogenized and spray dried.

The following specific Example illustrates the preparation of a compressed tablet in accordance with the invention.

EXAMPLE

Ingredients	Amounts Mg./Tablet
Antacid Layer	
Antacid (see below)	250—750
Glycine	50
Mannitol	350
Methylcellulose	24
Saccharin sodium, U.S.P.	3
Polyvinylpyrrolidone (5% in alcohol)	18
Magnesium stearate	14
Cornstarch	12
Flavor	q.s.
Organopolysiloxane Layer	
Spray dried organopolysiloxane Powder (Methylcellulose 2.5 mg., Milk solids 22.5 mg., Dimethylpolysiloxane 25 mg.)	50
Mannitol, N.F.	100
Glycine	50
Polyvinylpyrrolidone	5
Saccharin sodium	1
Magnesium stearate	12
Cornstarch	4
Flavor	q.s.

The antacid granulation is prepared by screening and mixing the antacid, glycine, mannitol and methylcellulose. The polyvinylpyrrolidone solution with the saccharin is then used as a granulating syrup. The granu-

lation is dried, screened and mixed with flavor, lubricant and disintegrant.

The organopolysiloxane layer is prepared identically using the ingredients described to form a granulation mixture. The organopolysiloxane layer may then be compressed to form a core in a standard tablet press with the antacid granulation then either press coated around the organopolysiloxane core or pressed onto the initial organopolysiloxane slug to form a two or three layered tablet.

Other tablet diluents such as lactose or sucrose may be used as well as other granulating agents which are used in alcoholic solution such as ethylcellulose. Other excipients or diluents known to the art may also be used.

WHAT WE CLAIM IS:—

1. A compressed tablet for the treatment of gastrointestinal disturbances, comprising pharmaceutically acceptable quantities of an antacid and a spray dried powdered organopolysiloxane composition, consisting of dry substantially spherical particles having a size from 5 microns to 1000 microns, each particle comprising a liquid organopolysiloxane substantially completely coated with from 15% to 95% by weight based on the particle of a nontoxic coating material selected from acacia, gum, guar gum, calcium caseinate, sodium caseinate, ammonium caseinate, milk solids, polyvinyl alcohol, polyvinylpyrrolidone, methylcellulose and carboxymethylcellulose, said organopolysiloxane constituting from 5% to 85% by weight of the particles.

2. A compressed tablet as claimed in Claim 1, wherein the antacid is magnesium aluminium oxyhydroxide, aluminium hydroxide dried gel, aluminium phosphate, calcium carbonate, magnesium carbonate, magnesium trisilicate, magnesium oxide, dihydroxy aluminium aminoacetate, magnesium hydroxide or a combination thereof.

3. A compressed tablet as claimed in Claim 1 or 2, wherein the organopolysiloxane is a dimethylpolysiloxane.

4. A compressed tablet as claimed in Claim 1, 2 or 3, wherein the coating material is milk solids.

5. A compressed tablet as claimed in Claim 1, 2 or 3, wherein the coating material is polyvinyl alcohol.

6. A compressed tablet as claimed in Claim 1, 2 or 3, wherein the coating material is calcium caseinate.

7. A compressed tablet as claimed in any preceding claim, wherein the organopolysiloxane powder and the antacid are separately contained in one or more layers or a coating.

8. A compressed tablet as claimed in Claim 7, wherein the tablet is a double or triple layer tablet of which at least one layer contains the antacid and at least one layer contains the organopolysiloxane powder.

9. A compressed tablet as claimed in any one of Claims 1 to 6, wherein the powdered organopolysiloxane composition and the antacid are mixed prior to compression.

10. A compressed tablet as claimed in any preceding claim, wherein the organopolysiloxane composition is a composition substantially as described in any one of the foregoing preparatory Examples A to H.

11. A compressed tablet for the treatment of gastrointestinal disturbances, substantially as described in the foregoing specific Example.

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